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A study on neurodevelopmental outcome and its associated risk factors in very low birth weight babies in a tertiary care teaching hospital in Kolkata

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ABSTRACT

Background: Very low birth weight babies are very fragile in nature and usually undergone through stormy neonatal period, which affects significantly their neurodevelopmental outcome in long term basis. **Aims and Objectives:** 1. Assessment of neurodevelopmental outcome in very low birth weight (VLBW) babies at 12 month corrected gestational age. 2. Study of risk factors associated with such outcome. **Materials and Methods:** VLBW babies without any major congenital anomaly were included in this study. They were followed up in high risk clinic upto 12 month corrected gestational age. In follow up visits, assessment of tone was done by Amiel Tieson method and 180 degree flip test. Developmental screening was done by Denver Developmental Screening Test (DDST II). Data obtained from this study were entered in Microsoft Excel and subsequently analysed with the help of Epi Info (TM) 3.5.3 software. **Results:** 24.4% among the study population showed neurodevelopmental abnormalities. Of them, 22.2% VLBW infants had muscle tone abnormality; 15.6% were suspect in gross motor development, 8.9% were suspect in fine motor, 11.1% were suspect in personal – social and 8.9% were suspect in language development, which were statistically significant. On assessment of risk factors, it was found that low birth weight, prematurity, non-use of antenatal corticosteroid, hypoglycaemia, intraventricular haemorrhage, sepsis, jaundice, mechanical ventilation, intra uterine growth retardation were significantly associated with various strata of neurodevelopmental outcome. **Conclusion:** VLBW babies are very prone to develop neurodevelopmental complications. Taking proper care regarding above said risk factors can reduce such complications. Also these babies should follow up properly to detect complication/s at earliest, and take "early intervention'' steps.

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INTRODUCTION

Very Low Birth Weight (VLBW) babies account for 3.4% of all live births according to the National Neonatal-Perinatal Database report 2002-2003.[1] Most of these high risk babies are born preterm and are prone to maladjustment to outside environment and suffer from various complications compared to term, normal birth weight babies. Many survivors face a lifetime of disability ranging from severe handicap such as cerebral palsy, cognitive impairment, blindness and hearing loss to impairment of short term memory, strabismus, language delays, learning difficulties and behavioural disorders.

As a part of follow up, periodic neurological and neuro behavioural assessment is essential in these high risk newborns. Early screening for hearing and visual impairment is imperative. Popularly used screening tests

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include DDST-I,[2] Denver II[3] and neuro motor evaluation by Amiel-Tison method.[4] Children who fail a screening test need close follow-up and additional assessment.

In a meta-analysis of 111 outcome studies of surviving VLBW infants, Escobar et al reported that the median incidence of cerebral palsy among all the cohorts studied was 7.7%, and the median incidence of disability was 25.0%.[5]

Abnormal tone has been found to be a good marker of neuromotor delay. Chaudhary et al found that assessment of tone by Amiel-Tison method at 3 month corrected gestational age was a good predictor of outcome at 12 month.[6]

The present study was conducted on VLBW (≤ 1500 gram) level III NICU graduate babies with an aim to evaluate their neurodevelopmental outcome at 12 months corrected age. Also the risk factors associated with such outcomes were assessed simultaneously.

METHODS

Study area

High Risk Clinic, Department of Paediatric Medicine, Vivekananda Institute of Medical Sciences (VIMS), Kolkata.

Study population

Newborn babies having birth weight below 1500 g. 68 babies were fulfilled this criteria initially; but 17 babies died before discharge. Out of rest 51 babies, 1 died during follow up period and 5 babies were lost in follow up. So, 45 babies had completed their follow up till 12 month corrected gestational age.

Exclusion criterion

Newborn with major congenital malformation.

Study period

Study was conducted during the period of February 2013 to January 2015.

Study design

Prospective observational study.

Study technique

68 newborn babies with birth weight less than 1500 g and without any associated congenital anomaly were picked up for this study. Informed consents were taken from their parents; all baseline data regarding their NICU stay were documented and advised for regular follow up following discharge. They were followed up at high risk clinic at 1 month, 2 month, 4 month, 8 month and 12 months of corrected age. Babies having dreaded complications like IVH, neonatal seizure, babies undergone exchange transfusion, were followed up more frequently and were asked to visit just 2 weeks after discharge.

In all follow up visits, anthropometry was done. Assessment of tone was done by Amiel Tieson method and 180 degree flip test. Developmental screening was done by Denver Developmental Screening Test (DDST II).

Data obtained from this study were entered in Microsoft Excel and subsequently analysed with the help of Epi Info (TM) 3.5.3 software.

Chi square test was used to test the association of different study variables in the study groups. Z-test (Standard Normal Deviate) was used to test the significant difference between two proportions. T-test was used to compare the means. Odds ratio (OR) with 95% Confidence Interval (CI) was calculated to measure the different risk factors. Fisher exact test was also applied to test the difference between the proportions. The significance level was set at 0.05 and confidence intervals were at 95 percent level.

Categorical variables are expressed as number of patients & percentage of patients. Continuous variables are expressed as Mean ± SD.

RESULTS

- Table 1 shows at 12 months corrected age, 75.6% VLBW infants had normal neurodevelopment and 24.4% showed neurodevelopmental abnormalities.
- 22.2% VLBW infants had muscle tone abnormality; 15.6% were suspect in gross motor development, 8.9% were suspect in fine motor, 11.1% were suspect in personal – social and 8.9% were suspect in language development (Table 2)
- Table 2 shows at 12 months corrected age, 77.8% of VLBW infants had normal tone and 22.2% had abnormal tone.
- 17.8% of VLBW infants had mild Hypertonia, 2.2% had mild Hypotonia and 2.2% had spastic quadriplegia (i.e., cerebral palsy) (Table 2).
- At 12 months corrected age, gross motor development of 84.4% VLBW infants was normal and 15.6% was suspect (Table 2).
- At 12 months corrected age, 8.9% VLBW infants was suspect in fine motor/adaptive development and 11.1% VLBW infants was suspect in personal – social development (Table 2).

- 91.1% VLBW infants had normal language development at 12 months corrected age and 8.9% infants was suspect in language development (Table 2).
- Table 3 shows risk of having abnormal tone was 3.40 times more for ELBW (<1000g) babies compared to babies in 1000 – 1499 g category [OR-3.40 (3.26, 14.18); p=0.0001] and the risk was significant.
- Gestational age < 30 weeks was significantly associated with risk of having abnormal tone (p=0.00001) (Table 3).

Table 1: Neurodevelopmental outcome at 12 months corrected age

Status	Number	Percentage
Normal	34	75.6
Neurodevelopmental abnormalities	11	24.4
• Muscle tone abnormality	10	22.2
• Suspect in gross motor development	7	15.6
• Suspect in fine motor development	4	8.9
• Suspect in personal-social development	5	11.1
• Suspect in language development	4	8.9

Table 2: Variables of neurodevelopmental outcome of VLBW infants under study at 12 months corrected age (n=45)

Characteristics	Number	Percentage	p-value
Tone			
Normal	35	77.8	
Abnormal	10	22.2	0.00001
Abnormal tone			
Mild hypertonia	8	17.8	
Mild hypotonia	1	2.2	0.013
Spastic quadruplagia	1	2.2	
Gross motor development			
Normal	38	84.4	
Suspect	7	15.6	0.000001
Fine motor development			
Normal	41	91.1	
Suspect	4	8.9	0.000001
Personal-social development			
Normal	40	88.9	
Suspect	5	11.1	0.000001
Language development			
Normal	41	91.9	
Suspect	4	8.9	0.000001

Table 3: Risk factors for neurodevelopmental outcome – Tone (n=45)

Risk factors	Category total	Normal tone (%)	Abnormal tone* (%)	p-value	Odds ratio	95% CI of OR
Birth weight						
<1000 g	6	1 (16.7)	5 (83.3)	0.0001	3.4	3.26, 14.18
1000-1499 g	39	34 (87.2)	5 (12.8)			
Gestational age						
<30 wks	9	2 (22.2)	7 (77.8)	0.00001	NA	NA
30-33 wks	31	29 (93.5)	2 (6.5)			
>33 wks	5	4 (80)	1 (20)			
Intra uterine growth						
AGA	26	20 (76.9)	6 (23.1)	0.84	1.12	0.26,4.70
SGA	19	15 (78.9)	4 (21.1)			
Antenatal corticosteroid						
Given	26	26 (100.0)	0 (0.0)	0.00002	NA	
Not given	19	9 (47.4)	10 (52.6)			
Apgar score at 5 min						
<6	7	1 (14.3)	6 (85.7)	0.00001	5.1	4.83,18.49
≥6	38	34 (89.5)	4 (10.5)			
Active resuscitation						
Done	10	2 (20.0)	8 (80.0)	0.000001	6.01	4.02,12.59
Not done	35	33 (94.3)	2 (5.7)			
Need for ventilation						
Yes	12	3 (25.0)	9 (75.0)	0.000001	9.12	8.87,25.19
No	33	32 (97.0)	1 (3.0)			
Hypoglycaemia						
Yes	7	1 (14.3)	6 (85.7)	0.00001	5.1	4.83,10.49
No	38	34 (89.5)	4 (10.5)			
Sepsis (culture/screen positive)						
Present	11	3 (27.3)	8 (72.7)	0.000004	2.66	1.07,9.82
Absent	34	32 (94.1)	2 (5.9)			
Neonatal jaundice						
Present	21	13 (61.9)	8 (38.1)	0.016	6.76	1.24,16.84
Absent	24	22 (91.7)	2 (8.3)			
Intervention						
Phototherapy	18	12 (66.7)	6 (33.3)	0.11	7	0.49,9.86
Exchange transfusion	3	1 (33.3)	2 (66.7)			
IVH						
Present	5	0 (0.0)	5 (100.0)	0.0002	NA	NA
Absent	40	35 (87.5)	5 (12.5)			

*Abnormal Tone includes Spastic, Hyper & Hypotonia

Table 4: Risk factors for neurodevelopmental outcome – Gross motor (n=45)

Risk factors	Category total	Normal gross motor (%)	Suspect gross motor (%)	p-value	Odds ratio	95% CI of OR
Birth weight						
<1000 g	6	0 (0.0)	6 (100.0)	0.0000008	NA	NA
1000-1499 g	39	38 (97.4)	1 (2.6)			
Gestational age						
<30 wks	9	4 (44.4)	5 (55.6)	0.0000001	NA	NA
30-33 wks	31	30 (96.8)	1 (3.2)			
>33 wks	5	4 (80.0)	1 (20.0)			
Intra uterine growth						
AGA	26	24 (92.3)	2 (7.7)	0.08	4.28	0.73,25.09
SGA	19	14 (73.7)	5 (26.3)			
Antenatal corticosteroid						
Yes	26	25 (96.2)	1 (3.8)	0.011	11.53	1.25,16.30
No	19	13 (68.4)	6 (31.6)			
Apgar score at 5 min						
<6	7	1 (14.3)	6 (85.7)	0.000001	2.22	1.21,4.04
≥6	38	37 (97.4)	1 (2.6)			
Active resuscitation						
Yes	10	4 (40.0)	6 (60.0)	0.00001	1.55	1.02,5.38
No	35	34 (97.1)	1 (2.9)			
Need for ventilation						
Yes	12	6 (50.0)	6 (50.0)	0.0001	3.24	1.21,5.86
No	33	32 (97.0)	1 (3.0)			
Hypoglycaemia						
Yes	7	3 (42.9)	4 (57.1)	0.0009	1.55	1.04,6.31
No	38	35 (92.1)	3 (7.9)			
Sepsis (culture/screen positive)						
Present	11	5 (45.5)	6 (54.5)	0.00004	3.96	1.90,15.85
Absent	34	33 (97.1)	1 (2.9)			
Neonatal jaundice						
Present	21	15 (71.4)	6 (28.6)	0.024	2.9	1.04,8.26
Absent	24	23 (95.8)	1 (4.2)			
Intervention						
Phototherapy	18	14 (77.8)	4 (22.2)			
Exchange transfusion	3	1 (33.3)	2 (66.7)	0.11	7	0.49,9.86
IVH						
Present	5	1 (20.0)	4 (80.0)	0.00002	4.33	1.01,9.33
Absent	40	37 (92.5)	3 (7.5)			

- AGA babies had 1.12 times risk of having abnormal tone as compared to SGA babies [OR-1.12 (0.26, 4.70)]; however the risk was not significant (p=0.84) (Table 3).
- Non-use of Antenatal Steroid was significantly associated with development of abnormal tone (p=0.00002) when compared to use of Antenatal Steroid (Table 3).
- The risk of having abnormal tone was 5.10 times more for Apgar score at 5 minutes < 6 [OR-5.10 (4.83, 18.49); p=0.00001] and the risk was significant (Table 3).
- The risk of having abnormal tone was 6.01 times more for Active resuscitation at birth [OR-6.01 (4.02, 12.59); p=0.000001], 9.12 times more for using Ventilation [OR-9.12 (8.87, 25.19); p=0.000001], 5.10 times more for Hypoglycaemia [OR-5.10 (4.83, 18.49); p=0.00001], 2.66 times more for Sepsis [OR-2.66 (1.07, 9.82); p=0.000004] and the risks were significant (Table 3).
- Neonatal Jaundice was significantly associated with development of abnormal tone [OR-6.76 (1.24, 16.84); p=0.016] (Table 3).
- The risk of developing abnormal tone was 4 times more for Exchange transfusion when compared to Phototherapy [OR-4 (0.29, 5.47)]; however the risk was not significant (p=0.27) (Table 3).
- IVH was significantly associated with development of abnormal tone (p=0.0002) (Table 3).
- Table 4 shows ELBW babies (birth weight <1000g) were significantly associated with suspect gross motor development (p=0.0000008).
- Gestational age <30 weeks was also significantly associated with suspect gross motor development (p=0.0000001) (Table 4).
- The risk of having suspect gross motor development was 4.28 times more for SGA babies compared to AGA babies [OR-4.28 (0.73, 25.09)]; however the risk was not significant (p= 0.08) (Table 4).
- Non-use of Antenatal Steroid carried 11.53 times risk of having suspect gross motor development when compared to using Antenatal Steroid [OR-11.53 (1.25, 16.30)] and the risk was significant (p= 0.011) (Table 4).

Table 5: Risk factors for neurodevelopmental outcome – Fine motor/adaptive (n=45)

Risk factors	Category total	Normal fine motor (%)	Suspect fine motor (%)	p-value	Odds ratio	95% CI of OR
Birth weight						
<1000 g	6	2 (33.3)	4 (66.7)	0.00005	NA	NA
1000-1499 g	39	39 (100.0)	0 (0.0)			
Gestational age						
<30 wks	9	6 (66.7)	3 (33.3)	0.015	NA	NA
30-33 wks	31	30 (96.8)	1 (3.2)			
>33 wks	5	5 (100.0)	0 (0.0)			
Intra uterine growth						
AGA	26	25 (96.2)	1 (3.8)	0.07	4.6	1.32,12.14
SGA	19	16 (84.2)	3 (15.8)			
Antenatal corticosteroid						
Yes	26	25 (96.2)	1 (3.8)	0.07	4.6	1.32,12.14
No	19	16 (84.2)	3 (15.8)			
Apgar score at 5 min						
<6	7	3 (42.9)	4 (57.1)	0.0001	NA	NA
≥6	38	38 (100.0)	0 (0.0)			
Active resuscitation						
Yes	10	6 (60.0)	4 (40.0)	0.0007	NA	NA
No	35	35 (100.0)	0 (0.0)			
Need for ventilation						
Yes	12	8 (66.7)	4 (33.3)	0.0001	NA	NA
No	33	33 (100.0)	0 (0.0)			
Hypoglycaemia						
Yes	7	5 (71.4)	2 (28.6)	0.06	7.2	0.82,13.17
No	38	36 (94.7)	2 (5.3)			
Sepsis (culture/screen positive)						
Present	11	7 (63.6)	4 (36.4)	0.0001	NA	NA
Absent	34	34 (100.0)	0 (0.0)			
Neonatal jaundice						
Present	21	17 (81.0)	4 (19.0)	0.025	NA	NA
Absent	24	24 (100.0)	0 (0.0)			
Intervention						
Phototherapy	18	16 (88.9)	2 (11.1)			
Exchange transfusion	3	1 (33.3)	2 (66.7)	0.14	6.1	0.95,8.23
IVH						
Present	5	2 (40.0)	3 (60.0)	0.00002	5.85	1.04,17.22
Absent	40	39 (97.5)	1 (2.5)			

- The risk of having suspect gross motor development was 2.22 times more for Apgar score at 5 minutes < 6 [OR-2.22 (1.21, 4.04); p=0.000001] and the risk was significant (Table 4).
- The risk of having suspect gross motor development was 1.55 times more for Active resuscitation at birth [OR-1.55 (1.02, 5.38); p=0.00001], 3.24 times more for using Mechanical Ventilation [OR-3.24 (1.21, 5.86); p=0.0001], 1.55 times more for hypoglycaemia [OR-1.55 (1.04, 6.31); p=0.0009], 3.96 times more for Sepsis [OR-3.96 (1.90, 15.85); p=0.00004] and the risks were significant (Table 4).
- Neonatal Jaundice was significantly associated with suspect gross motor development [OR-2.90 (1.04, 8.26); p=0.024] (Table 4).
- The risk of having suspect gross motor development was 7 times more for Exchange transfusion when compared to Phototherapy [OR-7.00 (0.49, 9.86)]; however the risk was not significant (p=0.11) (Table 4).
- The risk of having suspect gross motor development was 4.33 times more for IVH [OR-4.33 (1.01, 9.33)] and the risk was significant (p=0.00002) (Table 4).
- Table 5 shows ELBW babies (birth weight <1000g) were significantly associated with suspect fine motor development (p=0.00005).
- Gestational age <30 weeks was also significantly associated with suspect fine motor development (p=0.015) (Table 5).
- The risk of having suspect fine motor development for both SGA babies and non-use of Antenatal steroid was 4.6 times more [OR-4.6 (1.32, 12.14)]; however the risk was not significant (p= 0.07) (Table 5).
- Suspect fine motor development was significantly associated with Apgar score at 5 minutes <6 (p=0.0001), Active resuscitation at birth (p= 0.0007) use of mechanical ventilator (p= 0.0001), Sepsis (p= 0.0001) and Neonatal Jaundice needing treatment (p= 0.025) (Table 5).

Table 6: Risk factors for neurodevelopmental outcome – Personal - social (n=45)

Risk factors	Category total	Normal personal-social (%)	Suspect personal-social (%)	p-value	Odds ratio	95% CI of OR
Birth weight						
<1000 g	6	2 (33.3)	4 (66.7)	0.00004	7.6	2.57,14.35
1000-1499 g	39	38 (97.4)	1 (2.6)			
Gestational age						
<30 wks	9	6 (66.7)	3 (33.3)	0.032	NA	
30-33 wks	31	30 (96.8)	1 (3.2)			
>33 wks	5	4 (80.0)	1 (20.0)			
Intra uterine growth						
AGA	25 (96.2)	1 (3.8)	1 (3.8)	0.00004	0.06	0.01,1.47
SGA	19	15 (78.9)	4 (21.1)			
Antenatal corticosteroid						
Yes	25 (96.2)	1 (3.8)	1 (3.8)	0.00004	0.06	0.01,1.47
No	19	15 (78.9)	4 (21.1)			
Apgar score at 5 min						
<6	7	2 (28.6)	5 (71.4)	0.000008	NA	NA
≥6	38	38 (100.0)	0 (0.0)			
Active resuscitation						
Yes	10	5 (50.0)	5 (50.0)	0.00001	NA	NA
No	35	35 (100.0)	0 (0.0)			
Need for ventilation						
Yes	12	8 (66.7)	4 (33.3)	0.004	6.01	1.56,16.35
No	33	32 (97.0)	1 (3.0)			
Hypoglycaemia						
Yes	7	4 (57.1)	3 (42.9)	0.003	3.5	1.71,6.56
No	38	36 (94.7)	2 (5.3)			
Sepsis (culture/screen positive)						
Present	11	7 (63.6)	4 (36.4)	0.002	8.85	1.81,19.54
Absent	34	33 (97.1)	1 (2.9)			
Neonatal jaundice						
Yes	21	17 (81.0)	4 (19.0)	0.002	5.41	0.55,12.86
No	24	23 (95.8)	1 (4.2)			
Intervention						
Phototherapy	18	16 (88.9)	2 (11.1)			
Exchange transfusion	3	1 (33.3)	2 (66.7)	0.14	6.1	0.95,8.23
IVH						
Present	5	2 (40.0)	3 (60.0)	0.0002	8.5	2.89,28.15
Absent	40	38 (95.0)	2 (5.0)			

- The risk of having suspect fine motor development was 7.20 times more for hypoglycaemia [OR-7.20 (0.82, 13.17); p=0.06], and 5.85 times more for IVH [OR-5.85 (1.04, 17.22); p=0.00002] and the risks were significant (Table 5).
- The risk of having suspect fine motor development was 6.10 times more for Exchange Transfusion compared to Phototherapy [OR-6.10 (0.95, 8.23)], but the risk was not significant (p=0.14) (Table 5).
- Table 6 shows the risk of having suspect personal-social development was 7.60 times more for ELBW babies (<1000 g) compared to babies in 1000-1499 g category [OR-7.60 (2.57, 14.35)] and the risk was significant (p=0.00004).
- Suspect personal – social development was significantly associated with Gestational age < 30 weeks (p=0.032), Apgar score at 5 minutes < 6 (p=0.000008) and Active resuscitation at birth (P= 0.00001) (Table 6).
- The risk of having suspect personal - social development for both SGA babies and non-use of Antenatal steroid was 6.7 times more [OR-6.7 (4.04, 10.26)] and the risk was significant (p= 0.03) (Table 6).
- The risk of having suspect personal - social development was 6.01 times more for use of Mechanical Ventilation [OR-6.01 (1.56, 16.35); p=0.004], 3.50 times more for Hypoglycaemia [OR-3.50 (1.71, 6.56); p= 0.003], 8.85 times more for Sepsis [OR-8.85 (1.81, 19.54); p=0.002]5.41 times more for Neonatal Jaundice needing treatment [OR-5.41 (0.55, 12.86); p= 0.0002] and 8.50 times more for IVH [OR-8.50 (2.890, 28.15); p= 0.0002] and the risks were significant (Table 6).
- Exchange Transfusion had 6.10 times more risk of having suspect personal–social development compared to Phototherapy [OR-6.10 (0.95, 8.23)]; however the risk was not significant (p= 0.14) (Table 6).

Table 7: Risk factors for neurodevelopmental outcome – Language (n=45)

Risk factors	Category total	Normal language (%)	Suspect language (%)	p-value	Odds ratio	95% CI of OR
Birth weight						
<1000 g	6	2 (33.3)	4 (66.7)	0.00005	NA	NA
1000-1499 g	39	39 (100.0)	0 (0.0)			
Gestational age						
<30 wks	9	6 (66.7)	3 (33.3)	0.015	NA	NA
30-33 wks	31	30 (96.8)	1 (3.2)			
>33 wks	5	5 (100.0)	0 (0.0)			
Intra uterine growth						
AGA	26	25 (96.2)	1 (3.8)	0.0002	0.16	0.02,2.23
SGA	19	16 (84.2)	3 (15.8)			
Antenatal corticosteroid						
Yes	26	25 (96.2)	1 (3.8)	0.0002	0.16	0.02,2.23
No	19	16 (84.2)	3 (15.8)			
Apgar score at 5 min						
<6	7	3 (42.9)	4 (57.1)	0.0001	NA	NA
≥6	38	38 (100.0)	0 (0.0)			
Active resuscitation						
Yes	10	6 (60.0)	4 (40.0)	0.0007	NA	NA
No	35	35 (100.0)	0 (0.0)			
Need for ventilation						
Yes	12	8 (66.7)	4 (33.3)	0.001	NA	NA
No	33	33 (100.0)	0 (0.00)			
Hypoglycaemia						
Present	7	5 (71.4)	2 (28.6)	0.046	7.2	0.82,17.20
Absent	38	36 (94.7)	2 (5.3)			
Sepsis (culture/screen positive)						
Present	11	7 (63.6)	4 (36.4)	0.001	NA	NA
Absent	34	34 (100.0)	0 (0.0)			
Neonatal jaundice						
Present	21	17 (81)	4 (19)	0.001	NA	NA
Absent	24	24 (100.0)	0 (0.0)			
Intervention						
Phototherapy	18	16 (88.9)	2 (11.1)	0.0002	0.023	0.003,1.04
Exchange transfusion	3	1 (33.3)	2 (66.7)			
IVH						
Present	5	2 (40.0)	3 (60.0)	0.0002	8.51	2.04,26.14
Absent	40	39 (97.5)	1 (2.5)			

- Table 7 shows ELBW babies (< 1000 g) were significantly associated with suspect language development (p= 0000.5) when compared to babies in 1000 – 1499 g category.
- Gestational age < 30 weeks was also significantly associated with suspect language development (p=0.015) (Table 7).
- The risk of having suspect language development was 4.6 times more for both SGA babies and non-use of Antenatal Steroid [OR-4.6 (1.32, 12.14)]; however the risk was not significant (p= 0.07) (Table 7).
- Suspect language development was significantly associated with Apgar score at 5 minutes <6 (p=0.0001), Active resuscitation at birth (p= 0.0007), use of Mechanical Ventilation (p=0.001), Sepsis (p=0.001) and Neonatal Jaundice needing treatment (p=0.001) (Table 7).
- The risk of having suspect language development was 7.20 times more for Hypoglycaemia [OR-7.20 (0.82, 17.20); p=0.046], 8.51 times more for IVH [OR-8.51 (*2.04, 26.14); p=0.0002] and the risks were significant (Table 7).
- Exchange Transfusion had 6.10 times more risk of having suspect language development when compared to Phototherapy [OR-6.10 (0.95, 8.23)], however the risk was not significant (p=0.14) (Table 7).

DISCUSSION

Advances in neonatal care allow survival of very low birth weight preterm infants, who are prone to a range of long term complications in comparison to their term, normal birth weight counterparts.[7-9] These problems range from severe handicap such as cerebral palsy, cognitive impairment, blindness and hearing loss to impairment of short term memory, strabismus, language delays, learning difficulties and behavioural disorders.[7,10,11]

Individual children often have multiple disabilities[12] and those handicaps persist into school going age and beyond.[13] There is concern that improved rates of survival of very low birth weight (VLBW), and particularly extremely low birth weight (ELBW) infants, may be associated with increased rates of neurodevelopmental handicap.[14] It is increasingly important to study VLBW infants and provide longitudinal follow up after hospital discharge, to ensure early diagnosis of neurodevelopment abnormalities, enabling timely intervention for better quality of life.

In present study, cerebral palsy (CP) was diagnosed if the baby had spastic diplegia or hemiplegia or quadriplegia and suspect was assigned when mild hypotonia was persisting at corrected age 12 months.

Of the 45 VLBW babies who completed follow up till one year, 75.6% (n=34) had normal neurodevelopment and 24.4% (n=11) had neurodevelopmental abnormalities. 10 babies (22.2% of total) had abnormalities of muscle tone. Out of these 8 (17.8% of total) VLBW babies had mild hypertonia, 1 (2.2% of total) VLBW baby had mild hypotonia and 1 (2.2% of total) VLBW baby had spastic quadriplegia (diagnosed as CP). Mukhopadhyay, et al[15] reported 3% rate of CP among VLBW babies at corrected age 12 months which is similar to the present study. The report from a Malaysian nursery[16] also reported the CP rate of 3.9% in VLBW babies. There is a declining trend in CP rate amongst VLBW babies as reported by European database study[17] and the rate fell from 60.6 per 1000 live born VLBW infants in 1980 to 39.5 in 1996.

In the present study, 15.6% VLBW babies were suspect on DDST-II in gross motor development at 12 months of corrected age. One Indian study by Mukhopadhyay, et al[15] reported that gross motor development was delayed in 11% and questionable in 12.9% VLBW babies on DDST-I at 12 months corrected age. Their study also showed language delay to be 8% and questionable in another 8% cases. In the present study, 8.9% VLBW infants were suspect in language development at 12 months corrected age.

In the present study, birth weight < 1000 g, gestational age < 30 weeks, use of antenatal steroid, Apgar score at 5 minutes< 6, need for active resuscitation at birth, need for ventilation, hypoglycaemia, sepsis and presence of IVH had correlation with abnormal neurodevelopmental outcomes and their association with abnormal outcomes were statistically significant. These findings were similar to those reported in other studies where birth weight,[18] gestational age,[19] perinatal asphyxia,[20] neonatal sepsis,[21] IVH,[20,22] respiratory distress,[19] duration of assisted ventilation[18,23] have all been associated with adverse neurodevelopmental outcome in VLBW babies.

Developmental outcome was assessed in the present study by DDST II (Denver Development Screening Test). It is a screening test. A detailed development assessment should be performed on any baby screened positive for developmental delay. Most of the western studies used Bailey"s Scale of Infant Development (BSID)[24] which is a very elaborate but costly test. The most commonly used tool for detailed developmental assessment in Indian studies was DASII (Developmental Assessment Scale for Indian Children)[25] which was adapted to Indian children. Difference in assessment tools may be a reason for difference in results for neurodevelopmental outcome in the present study. Also the number of babies enrolled in the study was small. There was 10% follow up loss in this study. Age at final assessment in the present study was also early wherein minor neurological deficit may have been missed, as longer follow up duration is required to assess subtle cognitive deficits, behavioural disorders and scholastic performance.

To conclude, VLBW babies are at high risk of developing neurodevelopmental complications. Use of antenatal corticosteroid; appropriate use of resuscitation steps; prompt management of hypoglycaemia, sepsis, neonatal jaundice can be beneficial regarding neurodevelopmental outcome. Besides that, these babies should undergo proper and timely follow up to detect neurodevelopmental complication/s at earliest and take necessary 'early intervention/s', so that they can live a favourable life in future.

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SS - Manuscript preparation, data collection, review of literature; **SD -** Statistical analysis, interpretation, literature search, review of study; **SM -** Concept, design of study, review of study, revision of manuscript.

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